**FULL STUDY TITLE**

**SHORT STUDY TITLE**

**CONFIDENTIAL**

This document is confidential and the property of XXX

No part of it may be transmitted, reproduced, published, or used without prior written authorisation from the institution.

# STATEMENT OF COMPLIANCE

This document is a protocol for a clinical research study. The study will be conducted in compliance with all stipulations of this protocol, the conditions of ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95).

**IMPORTANT NOTES:**

* **Please ensure you have engaged all persons relevant to your project including heads of department of all related departments. This can significantly reduce delays throughout the approval process.**
* **Please note that the HREC approval process can take a number of months. Please allow plenty of time.**
* **This template is to be used as a guide and will need to be modified to suit your study. Not all sections may apply.**
* **Please contact the Research Ethics Manager for guidance on ethical issues specific to your research.**
* **Information provided in the HREA must be consistent with the protocol.**
* **Please remove guidance text prior to submission (Red and highlighted text)**
* **Please complete the Ethics Checklist on the SESLHD Research Office website, and submit with your application.**
* **Submissions must be made via REGIS. Please see** [**https://regis.health.nsw.gov.au/how-to/**](https://regis.health.nsw.gov.au/how-to/)
* **Research cannot commence until both HREC approval *and* site / SSA authorisation are in place. Please contact the Research Office at your study sites if this is unclear.**

Contents

[**STATEMENT OF COMPLIANCE 1**](#_Toc69214690)

[**GLOSSARY OF ABBREVIATIONS 4**](#_Toc69214691)

[**1. Study Management 4**](#_Toc69214692)

[**2. INTRODUCTION AND BACKGROUND 5**](#_Toc69214693)

[**2.2 Research Question 5**](#_Toc69214694)

[**Clearly state the question the study intends to answer. 5**](#_Toc69214695)

[**2.3 Rationale for Current Study 5**](#_Toc69214696)

[**3 STUDY OBJECTIVES 5**](#_Toc69214697)

[**4. STUDY DESIGN 5**](#_Toc69214698)

[**5. STUDY TREATMENTS 6**](#_Toc69214699)

[**5.1 Treatment Arms 6**](#_Toc69214700)

[**5.1.1 Description 6**](#_Toc69214701)

[**5.1.2 Dosage and Route of Administration 6**](#_Toc69214702)

[**5.2 Preparation and administration of study drug 6**](#_Toc69214703)

[**5.3 Measurement of participant compliance 6**](#_Toc69214704)

[**5.4 Excluded medications and treatments 6**](#_Toc69214705)

[**6. PARTICIPANT ENROLLMENT AND RANDOMISATION 6**](#_Toc69214706)

[**6.3 Informed Consent Process 7**](#_Toc69214707)

[**7. STUDY VISITS AND PROCEDURES SCHEDULE 8**](#_Toc69214708)

[**Study Flow Chart 8**](#_Toc69214709)

[**8. CLINICAL AND LABORATORY ASSESSMENTS 9**](#_Toc69214710)

[**9. SERIOUS ADVERSE EVENT (SAE) REPORTING 9**](#_Toc69214711)

[**10. Significant Safety Issues (SSI) implemented as an Urgent Safety Measure (USM) Reporting 9**](#_Toc69214712)

[**11.1 Definitions 10**](#_Toc69214713)

[**11.3 Eliciting Serious Adverse Event Information 10**](#_Toc69214714)

[**11.4 Serious Adverse Event Reporting 10**](#_Toc69214715)

[**11.4.1 SAEs 10**](#_Toc69214716)

[**11.4.1 USADEs 10**](#_Toc69214717)

[**11.4.2 URSAE 11**](#_Toc69214718)

[**11.4.3 SUSARs 11**](#_Toc69214719)

[**12. STATISTICAL METHODS 11**](#_Toc69214720)

[**12.1 Sample Size Estimation 11**](#_Toc69214721)

[**12.2 Population to be analysed 11**](#_Toc69214722)

[**12.3 Statistical Analysis Plan 11**](#_Toc69214723)

[**12.4 Interim Analyses 11**](#_Toc69214724)

[**13. DATA MANAGEMENT 11**](#_Toc69214725)

[**14. ADMINISTRATIVE ASPECTS 12**](#_Toc69214726)

[**15. USE OF DATA AND PUBLICATIONS POLICY 12**](#_Toc69214727)

[**16. REFERENCES 13**](#_Toc69214728)

[**17. APPENDICES 13**](#_Toc69214729)

PROTOCOL SYNOPSIS

|  |  |
| --- | --- |
| Title |  |
| Objectives | Primary:  Secondary: |
| Study Design |  |
| Study Sites |  |
| Planned Sample Size |  |
| Selection Criteria |  |
| Study Procedures |  |
| Statistical Procedures | Sample Size Calculation:  Analysis Plan: |
| Duration of the study |  |

# GLOSSARY OF ABBREVIATIONS

|  |  |
| --- | --- |
| **ABBREVIATION** | **TERM** |
|  |  |
|  |  |
|  |  |

# Study Management

* 1. **Coordinating Principal Investigator**

The coordinating principal investigator is;

a) In relation to a clinical trial conducted at a single trial site, the investigator1 for that site; or

b) In relation to a clinical trial conducted at more than one trial site, the health professional, whether or not he or she is an investigator at any particular site, who takes primary responsibility for the conduct of the trial.

More info in link below

[**https://www.medicalresearch.nsw.gov.au/app/uploads/2018/04/ACTJWG-resp-investigator.pdf**](https://www.medicalresearch.nsw.gov.au/app/uploads/2018/04/ACTJWG-resp-investigator.pdf)

• Position

• Designation

• Institutional Email Address

• Phone

• Address

• Roles and responsibilities relevant to this research

* 1. **Principal Investigator/s**

The principal investigator (PI) is the person responsible, individually or a leader of the researchers at a site, for the conduct of a trial at that site. In a single centre trial, the principal investigator may also be the coordinating principal investigator.

If the research is multi-site, please include all investigators across all sites.

**•** Position

• Designation

• Institutional Email Address

• Phone

• Address

• Roles and responsibilities relevant to this research

* 1. **Associate Investigator/s**

• Position

• Designation

• Institutional Email Address

• Phone

• Address

• Roles and responsibilities relevant to this research

* 1. **Statistician**

Please include the name and title, contact information.

* 1. **Internal Trial Committees**
  2. **Independent Safety and Data Monitoring Committee**

Describe the membership and responsibilities – refer to [NHMRC guidance](https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods) on Data Safety Monitoring Boards. The [Murdoch Children’s Research Institute guidance](https://www.mcri.edu.au/images/documents/migrate/mctc_guidance_dsmb_final.pdf) (VIC) may also be useful.

* 1. **Sponsor**

The study sponsor is not necessarily the same as the funding body.

**The sponsor is the company, institution or organisation that takes overall responsibility for the conduct of the trial and usually initiates, organises and supports the clinical trial**. The sponsor usually owns the study protocol and study data.

Queries regarding sponsorship should be directed to the Research Office at your institution.

* 1. **Funding and resources**

Please explain all sources of funding/resources for this project, including in kind support (i.e. non-financial costs of personnel time etc).

Please note that a budget document will likely be required as part of your site specific application (SSA) for any NSW Health sites.

# INTRODUCTION AND BACKGROUND

# [Please See National Statement on Ethical Conduct In Human Research – Chapter 3](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018)

* 1. **Background Information**

Include information based on literature review and investigators’ experiences, brief history of the disease including prognostic factors. All references must be listed at the back of the protocol.

* 1. **Research Question**

Clearly state the question the study intends to answer (e.g. *‘In infants born prematurely, compared to those born at full term, what is the lifetime prevalence of sensory deafness?'*).

* 1. **Rationale for Current Study**

The rationale specifies the reasons for conducting the research in light of current knowledge. It should include a well-documented statement of the need/problem that is the basis of the project, the cause of this problem and its possible solutions. It is the equivalent to the introduction in a research paper and it puts the proposal in context. It should answer the question of why and what: why the research needs to be done and what will be its relevance.

# STUDY OBJECTIVES

Your research question needs to be further refined into one or more study objectives. The study objective(s) should be single and quantifiable statement(s) that will allow you to answer your research question. Objectives should be simple, specific, and stated in advance, (*e.g. to determine if socioeconomic status is associated with excess childhood asthma in Istanbul).*

* 1. **Primary Objective**
  2. **Secondary Objectives**

# STUDY DESIGN

**4.1 Type of Study**

For example a randomised control trial.

* 1. **Study Design**

The scientific integrity of the study and the credibility of the study data depend substantially on the study design and methodology. The methodology section is the most important part of the protocol. It should include detailed information on the interventions to be made, procedures to be used, measurements to be taken, observations to be made, laboratory investigations to be done etc. The design of the study should include information on the type of study, the research population or the sampling frame, and who can take part (e.g. inclusion and exclusion criteria, withdrawal criteria etc.), and the expected duration of the study

* 1. **Number of Participants**

Please state how many participants are to be included. If the study does not involve active human participation, please specify data from how many individuals is expected to be collected/ used.

* 1. **Study sites**

Enter all study sites and the expected number of participants at each site.

If the study involves a number of sites, make clear what occurs at each site.

* 1. **Expected Duration of Study**

Expected start and stop date.

Include the expected time period for the recruitment phase of the study and the expected time period for the follow up phase of the study.

* 1. **Primary and Secondary Outcome Measures**

The **primary outcome** should be the most important and clinically relevant outcome (e.g. clinical, psychological, economic, or other) of the study. This is the measure used to answer your study aim. It is also the outcome used to calculate study sample size and power. (e.g. caesarean/no caesarean; blood loss ≥500mL/blood loss <500mL; weight - kg; pain - mild, moderate, severe; time to event (e.g. survival); and counts (e.g. number of infections).

**Secondary outcome(s)** are measures of additional or less important research interest. They may include additional clinical, psychological, economic, or safety outcomes (e.g. treatment related side effects/adverse events). However, as these endpoints are not used to calculate study power and sample size it is often not possible to draw robust conclusions from the results.

# STUDY TREATMENTS

* 1. **Treatment Arms**

**5.1.1 Description**

**5.1.2 Dosage and Route of Administration**

* + 1. **Dose modification**
  1. **Preparation and administration of study drug**
     1. **Dispensing and Product Accountability**
  2. **Measurement of participant compliance**
  3. **Excluded medications and treatments**

# PARTICIPANT ENROLLMENT AND RANDOMISATION

* 1. **Recruitment**

Explain how potential participants will be identified for the study, where and by whom.

Explain how potential participants will be screened for the study.

# [Please See National Statement On Ethical Conduct In Human Research – Chapter 3](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) – Element 2 (Recruitment)

* 1. **Eligibility Criteria**
     1. **Inclusion Criteria**

List each criterion, eg. gender, age range, weight, height, disease status, laboratory parameters.

* + 1. **Exclusion Criteria**

List each criterion, eg:

* Women lactating, pregnant or of childbearing potential who are not willing to avoid pregnancy during the study
* Patients with a history of xxx disease(s) that is (are) likely to interfere with the metabolism or excretion of the test medication
* Patients who had an investigational new drug within the last xx days /weeks
* Patients with a history of psychological illness or condition such as to interfere with the patient’s ability to understand the requirements of the study.
* Patients with xxx disease that is likely to interfere with the evaluation of the patient’s safety and of the study outcome.

List the prohibited concomitant medications.

## Informed Consent Process

Describe consent procedures. The following fundamental conditions for a valid informed consent should be met for each participant: Disclosure of relevant information, comprehension of the information provided, voluntary agreement of the participant (free from coercion). State who will obtain consent. When obtaining consent, the “arm’s length” principle should be adhered to where possible to reduce potential for coercion.

[Please see National Statement on Ethical Conduct in Human Research – Chapter 3](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) – Element 3 (Consent)

* 1. **Enrolment and Randomisation Procedures**

Explain how a potential participant will be enrolled into the study (I.e. The participant will be enrolled into the study after the informed consent process has been completed and the participant has met all inclusion criteria and none of the exclusion criteria. The participant will receive a study enrolment number and this will be documented in the participant’s medical record and on all study documents.)

Please describe how randomisation (if applicable) will occur.

* 1. **Blinding Arrangements**

As relevant, provide information on how the study will be blinded. Provide a description of stopping rules for individuals, for part of the study or entire study, the procedures and conditions for breaking the codes etc. should also be described.

* 1. **Breaking of the Study Blind**
     1. **On Study**
     2. **Following Completion of the Study**
  2. **Participant Withdrawal**
     1. **Reasons for withdrawal**
     2. **Early termination**

List any possible circumstances that may lead to early termination of the study and outline how this will be managed, i.e. who will be responsible for what in the process of terminating the study (informing participants, correspondence to HREC, compiling a final study report, unblinding if applicable)?

* + 1. **Handling of withdrawals and losses to follow-up**
    2. **Replacements**
  1. **Trial Closure**

Outline any follow up that will be provided to the research participants and for how long. This may include a follow up, especially for adverse events, even after data collection for the research study is completed.

* 1. **Continuation of therapy**

Make clear any arrangements to allow continued access to study treatment after study completion.

# STUDY VISITS AND PROCEDURES SCHEDULE

## Study Flow Chart

Diagram of the study design (example below)

Enrolment

Randomisation

Treatment Phase

(e.g. 12 weeks)

Group A Group B

Include all study visits and all study procedures conducted at each visit. This information can also be displayed in a table.

Example below

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| List Interventions | Enrolment Visit | Visit 1 | Visit 2 | Visit 3 | Final Study Visit |
| Informed Consent | ✓ |  |  |  |  |
| Inclusion / Exclusion criteria | ✓ |  |  |  |  |
| Physical examination |  | ✓ |  |  |  |
| CXR | ✓ |  |  |  | ✓ |
| SAE /SSI/ USM/ USADE/SUSAR or URSAE Assessment |  | ✓ | ✓ | ✓ | ✓ |

If a study procedure will not performed as per normal practice, please outline how the procedure will be performed for this study.

Please make clear if any procedures form part of usual care (i.e. would be performed irrespective of participation in this trial).

# CLINICAL AND LABORATORY ASSESSMENTS

# SAFETY REPORTING:

# MANAGEMENT and REPORTING

Please define adverse events and detail how information will be elicited from patients and how adverse events will be managed.

Please see [Policy Directive - Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Public Health Organisations](https://www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2017_039.pdf) regarding reporting of adverse events for trials in NSW.

* 1. **Serious Breach Reporting**

Please see [NHMRC guidance](https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods) ‘Reporting of Serious Breaches of Good Clinical Practice (GDP) or the Protocol for Trials Involving therapeutic Goods’

Serious Breaches will be submitted to the HREC for review.

Serious Breach definition; A breach of Good Clinical Practice or the protocol that is likely to affect to a significant degree;

a) The safety or rights of a trial participant, or

b) The reliability and robustness of the data generated in the clinical trial.​

Serious breaches must be reported by the sponsor through the CPI within 7 calendar days of the breach. The breach must be submitted via Regis.

* 1. **Specific Safety Considerations (Eg. Radiation, Toxicity)**

Radiation risks outlined in the **Code of Practice** from the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) must be followed for all Exposure of Humans to Ionizing Radiation for Research Purposes.

[***www.arpansa.gov.au/Publications/codes/rps8.cfm***](http://www.arpansa.gov.au/Publications/codes/rps8.cfm)

The following should be detailed:

* Why the participants are exposed to ionizing radiation.
* The number of participants to be exposed.
* The precautions to be taken to keep exposure to a minimum.
* The exposure to radiation needs to be addressed with a formal **Radiation Safety Report.**

# STATISTICAL METHODS

* 1. **Sample Size Estimation**
  2. **Population to be analysed**
  3. **Statistical Analysis Plan**
  4. **Interim Analyses**

**Please do not submit an HREC application until your statistical methods are finalised.**

The statistical methods proposed to be used for the analysis of data should be clearly outlined, including reasons for the sample size selected, power of the study, level of significance to be used, procedures for accounting for any missing or spurious data etc. For projects involving qualitative approaches, specify in sufficient detail how the data will be analysed.

# DATA MANAGEMENT

Please see [National Statement on Ethical Conduct in Human Research](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) – Chapter 3 – Element 4 (Collection, Use and Management of Data and Information)

And [Management of Data and Information in Research (NHMRC)](https://www.nhmrc.gov.au/sites/default/files/documents/attachments/Management-of-Data-and-Information-in-Research.pdf)

* 1. **Data Collection**

Detail all sources of data to be collected, how the data will be collected, and by whom. Please include a list of all data points to be collected (a separate spreadsheet may be provided with your application if the number of points is extensive).

If you are sending data/specimens to an external organisation (outside of your organisation) please list organisation and describe how the transfer will occur.

**REDCap (Research Electronic Data Capture)** is a secure, web-based data capture and data management software tool designed for research purposes. RedCap is SESLHD HREC’s preferred data management software.

For SESLHD researchers, RedCap can be accessed via <https://redcap.sesi.health.nsw.gov.au/> or by contacting SESLHD-REDCap-admin@health.nsw.gov.au. Data collected by REDCap is stored on SESLHD servers.

* 1. **Data Storage**

Outline where and how the data will be securely stored (i.e. RedCap). Describe all procedures for handling data, how data are coded, who will be responsible for the data, who has access to the source data and database, by whom the key to the code is safeguarded (and separately stored), what steps will be taken to ensure data security, and how the participants’ privacy is protected, such as de-identification (more detail to be provided below). If the research is multi-site and data storage methods may differ across sites, please include this detail here.

* 1. **Data Confidentiality**

Explain how participants’ privacy will be protected and how data confidentiality will be maintained **during the study, for archiving and storage, and for publication**. Specify if data/records will be identifiable, re-identifiable (ie. coded), or de-identified/anonymised.

Please note that de-identified data is data that can never be re-identified.

With your submission, please include a separate data sheet showing all data points to be collected.

[**https://www.ipc.nsw.gov.au/fact-sheet-de-identification-personal-information**](https://www.ipc.nsw.gov.au/fact-sheet-de-identification-personal-information)

* 1. **Study Record Retention**

Per [Management of Data and Information in Research (NHMRC)](https://www.nhmrc.gov.au/sites/default/files/documents/attachments/Management-of-Data-and-Information-in-Research.pdf)

In general, the minimum period for retention of research data is 5 years from the date of publication. However, for any particular case, the period for which the data should be retained should be determined by the specific type of research, subject to any applicable state, territory or national legislation.

For example: • for short-term research projects that are for assessment purposes only, such as research projects completed by students, retaining research data for 12 months after the completion of the project may be sufficient

• for most clinical trials, retaining research data for 15 years or more may be necessary

• for areas such as gene therapy, research data must be retained permanently (e.g. data in the form of patient records)

• if the work has community, cultural or historical value, research data should be kept permanently, preferably within a national collection.

Please also outline how data will be securely destructed after the retention period has lapsed.

# ADMINISTRATIVE ASPECTS

All clinical trials must be registered in a publicly accessible trials registry prior to enrolment of the first participant. This is the responsibility of the investigator. If possible, you should include the registration number here.

* 1. **Independent HREC approval**

This study has been approved by the South Eastern Sydney Local Health District HREC 202X/ETHXXXXX:

* 1. **Amendments to the protocol**

Any amendments will be submitted via REGIS for review prior to implementation as per HREC guidelines.

Please see <https://regis.health.nsw.gov.au/how-to/> . Go to: Applicants – Quick Reference Guides or Walk through Videos – Ethics Post Approval – Completing and submitting Ethics Amendment

* 1. **Participant reimbursement**

Details of participant reimbursement, if any.

See [National Statement](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) 2.2.10

* 1. **Financial disclosure and conflicts of interest**

Details of any conflicts of interest and how they will be addressed.

# USE OF DATA AND PUBLICATIONS POLICY

The protocol should specify not only dissemination of results in the scientific media, but also to the community and/ or the participants, and consider dissemination to the policy makers where relevant. Publication policy should be clearly discussed- for example who will take the lead in publication and who will be acknowledged in publications, etc.

Please also clarify here if the study is for a student’s (including Honours and Postgraduate) project.

Please see [National Statement on Ethical Conduct in Human Research](https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) – Chapter 3 – Elements 5 and 6 (Communication of research results to participants and Dissemination of study outcomes)

# REFERENCES

This is the bibliography section for any information cited in the protocol.

List MUST INCLUDE: national and international guidelines on the conduct of research in humans (eg National Statement).